Addendum to October 31, 2024 Letter From FDA

January 31, 2025

Marie Kirby, PhD
Team Lead
Genomics and Diagnostics Team
DDID/NCIRD/Influenza Division
Centers for Disease Control and Prevention
pbi0@cdc.gov

Dear Dr. Kirby,

By email dated January 6, 2025, CDC requested an extension of the enforcement discretion for the use of conjunctival specimens with the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel, Influenza A/H5 Subtyping Kit (Ver 4) (K200370) that was described in FDA's May 23, 2024 letter and amended in FDA's October 31, 2024 letter. In response to CDC's request, FDA currently intends to exercise the enforcement discretion through May 1, 2025, or as otherwise determined by FDA that an earlier or later time period is appropriate while we continue to assess the situation and policy.

Sincerely,

Courtney H. Lias -S

Courtney H. Lias, Ph.D.
Director
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosures:

1) Copy of FDA Letter to CDC Dated October 31, 2024
2) Copy of FDA Letter to CDC Dated May 23, 2024

Addendum to July 31, 2024 Letter From FDA

October 31, 2024

Marie Kirby, PhD
Team Lead
Genomics and Diagnostics Team
DDID/NCIRD/Influenza Division
Centers for Disease Control and Prevention
pbi0@cdc.gov

Dear Dr. Kirby,

By email dated October 15, 2024, CDC requested an extension of the enforcement discretion for the use of conjunctival specimens with the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel, Influenza A/H5 Subtyping Kit (Ver 4) (K200370) that was described in FDA's May 23, 2024 letter and which was extended via FDA's July 31, 2024 letter. And as reflected in an October 21, 2024 email, CDC has requested a modification of such enforcement discretion, asking that FDA modify the existing risk mitigations described in the May 23, 2024 letter to include paired testing of additional specimen types based on recent confirmed influenza H5 cases in California where combined oropharyngeal swab (OPS)/anterior nasal swab (ANS) samples were positive in cases where nasopharyngeal swabs were negative. For the reasons described in FDA's May 23, 2024 letter and in light of this new information, at this time FDA does not intend to object to the continued use of conjunctival specimens with the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel, Influenza A/H5 Subtyping Kit (Ver 4) (K200370), with the adoption of the following risk mitigations:

- Testing of conjunctival specimens will be paired with testing of respiratory specimens collected using NPS and/or combined oropharyngeal (OPS)/anterior nasal swab (ANS) specimen type(s), which will mitigate the risks associated with the misdiagnosis of patient cases presenting with conjunctivitis and no correlating respiratory symptoms;

- The conjunctival specimens will be collected and transported using the same swabs and transport media as are NPS used with the currently cleared CDC kit; and

- CDC will notify FDA of any complaints received regarding the performance of the assay when conjunctival swabs are used within 7 days of receipt of the complaint.

[Continued on page 2]

FDA currently intends to exercise this enforcement discretion through February 1, 2025, or as otherwise determined by FDA that an earlier or later time period is appropriate while we continue to assess the situation and policy.

Sincerely,

Courtney H. Lias, Ph.D.
Director
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

May 23, 2024

John R. Barnes, PhD
Deputy Branch Chief for Science (Acting)
Virology Surveillance and Diagnosis Branch
DDID/NCIRD/Influenza Division
Centers for Disease Control and Prevention
fzq9@cdc.gov

Dear Dr. Barnes,

During the week of March 25, 2024, the U.S. Department of Agriculture (USDA) confirmed the detections of influenza A H5 highly pathogenic avian influenza (HPAI) in dairy cattle in the panhandle region of Texas. On April 1, 2024, the State of Texas announced that a person had tested positive for influenza A H5 HPAI. The patient reported eye redness as their only symptom, consistent with conjunctivitis. Conjunctivitis, although an uncommon symptom associated with influenza infections, is a known symptom associated with infection by HPAI (ex. Koopmans *et al.* Transmission of H7N7 avian influenza A virus to human beings during a large outbreak in commercial poultry farms in the Netherlands - PubMed (nih.gov) and Update on Avian Influenza A (H5N1) Virus Infection in Humans | New England Journal of Medicine (nejm.org)) and was the primary symptom in the H7N7 outbreak in the Netherlands.

Both respiratory (NP) and conjunctival specimens from the patient were tested with the CDC Human Influenza Virus Real-time RT-PCR, Influenza A/H5 Subtyping Kit (Ver 4) (K200370), and results indicated that both specimens were presumptive positive for influenza A(H5) virus and confirmed as HPAI using diagnostic RT-PCR and sequencing. The CDC Flu rRT-PCR Dx Panel Influenza A/H5 Subtyping Kit (Ver 4) (K200370) is currently 510(k) cleared for qualitative detection of influenza viruses in upper respiratory tract clinical specimens (including nasopharyngeal swabs (NPS) and lower respiratory tract specimens from human patients with signs and symptoms of respiratory infection and/or from viral culture.

In a letter dated May 3, 2024, CDC requested temporary enforcement discretion through August 1, 2024, for the use of conjunctival swabs as a specimen type with the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel, Influenza A/H5 Subtyping Kit (Ver 4) (K200370).

FDA understands that there is an urgent need to test conjunctival swabs given the current status of HPAI in the U.S. and that temporary enforcement discretion will among other things help CDC to better understand the new infection paradigm and collect positive and negative clinical conjunctival specimens for use in future studies. To support use of the new specimen type, CDC has provided bridging study data demonstrating the equivalency of conjunctival swabs to specimen types for which the assay (K200370) is already cleared for use. CDC further noted that the Ct value of the conjunctival swab (18) was significantly higher than the Ct value of the NP swab (33).

Consistent with the letter from CDC dated May 3, 2024, and in light of the uniqueness of the presentation of symptoms of HPAI and the urgent need to test conjunctival specimens using the CDC assay, at this time FDA does not intend to object to the use of conjunctival specimens with the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel, Influenza A/H5 Subtyping Kit (Ver 4) (K200370), with the adoption of the following risk mitigations:

- Testing of conjunctival specimens will be paired with testing of respiratory specimens collected using NPS, which will mitigate the risks associated with the misdiagnosis of patient cases presenting with conjunctivitis and no correlating respiratory symptoms;

- The conjunctival specimens will be collected and transported using the same swabs and transport media as are NPS used with the currently cleared CDC kit; and

- CDC will notify FDA of any complaints received regarding the performance of the assay when conjunctival swabs are used within 7 days of receipt of the complaint.

FDA currently intends to exercise this enforcement discretion through August 1, 2024, or as otherwise determined by FDA that an earlier or later time period is appropriate.

Sincerely,

Courtney H. Lias, Ph.D.
Acting Director
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health